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Ruthenium catalysed C-H bond borylation[†]

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An easily prepared series of phenylindenyldihydridosilyl ruthenium complexes (2a–2d) was obtained by reaction of tertiary silanes with the commercially-available [RuCl(3-phenylindenyl)(PPh₃)₂] (1). The [RuH₂(3-phenylindenyl)(SiEt₃)] (2a) complex was shown to be highly efficient (1.5 mol%) in the *ortho*-selective borylation of pyridyl substrates, with yields of up to 90%. A novel ruthenium(n)-catalysed C–H activation borylation/functionalization reaction using a remarkably low catalyst loadings is described.

Organosilicon ruthenium complexes have attracted significant attention due to their potential use as catalysts enabling the transformation of silane reagents in processes such as hydrosilylation, dehydrogenative polymerization and silane redistribution reactions.¹ For example, Nikonov has reported the hydrosilylation of carbonyl moieties using $[RuCp(P^iPr_3)(NCMe)(\eta^2-HSiR_3)]$.^{1d}

A plethora of silicon ruthenium complexes can be found in the literature. Most relevant to the work presented here, in 1988 Tilley described the synthesis of $[RuCp^*H_2(PhSiH_2)(P^iPr_3)]^2$ using PhSiH₃. Subsequently, the synthesis and catalytic applications of half-sandwich hydridosilyl ruthenium complexes was widely developed.³ In 2011, Tilley and coworkers following on seminal work of Caulton^{3d} described a family of dihydridopentamethylcyclopentadienyl ruthenium complexes $[RuCp^*(H)_2(SiRR'OTf)(P^iPr_3)]$, as intermediates in the synthesis of silylene ruthenium species.^{3h} This procedure required the synthesis of a key Ru-OTf bearing complex to access the desired hydridosilyl ruthenium complexes, as limited reactivity was exhibited by $[RuClCp^*(P^iPr_3)]$ with primary silanes.

Despite the interest and the significant potential of these hydridosilyl ruthenium complexes, methods for their preparation have remained limited. Their isolation requires usually multistep synthetic approaches,^{3a,c,d,f,h} that suffer from limitations regarding

the nature of the silane used, 3^{a-g} especially the lack of a synthetic route using the very common tertiary silanes.

In this context and taking into account the lack of simple synthetic protocols leading to hydridosilyl ruthenium complexes, we were pleased to discover that $[RuCl(PPh_3)_2(3\text{-phenylindenyl})]^4$ (1) when simply heated in toluene in the presence of tertiary silanes (2a-2e), allowed for easy access to a new family of 3-phenylindenyl dihydridosilyl ruthenium complexes in good yields (Scheme 1).

The complexes were fully characterized by spectroscopic techniques and elemental analysis confirms bulk purity of **2**. Of note, the ¹H-NMR spectra of **2** reveal various patterns in the hydride region as a function of the silyl group. This can be attributed to conformational interchanges of the hydrides about the ruthenium centre associated with silane electronic and steric properties.^{3c} To unequivocally establish the atom connectivity in **2**, the molecular structure of **2a** was elucidated by X-ray⁵ diffraction analysis of a single crystal (see ESI[†]).

The mechanism of formation of **2**, presumably occurs *via* oxidative addition of the Si–H bond of the silane to ruthenium associated with a PPh₃ ligand displacement. The potential reversible binding of the silane, *via* reductive elimination, prompted us to investigate whether complexes **2** could be active in C–H activation reactions, more specifically in the arene C–H bond borylation reactions.

The borylation of arenes through direct C-H activation has become a very straightforward and attractive route for the preparation of boron-containing reagents, excluding the need



Scheme 1 Synthesis of [RuH₂(SiR₃)(PPh₃)(3-phenylindenyl)] (2a-e).

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for the corresponding halides as intermediates.⁶ In 1999 and 2000, Smith and co-workers⁷ described the direct arene borylation catalysed by rhodium and iridium catalysts using pinacolborane. Hartwig, Miyaura and co-workers established the first direct arene borylation catalysed by an iridium catalyst in the presence of a bipyridine ligand using bis(pinacolato)diboron.⁸ The [Ir]/dtbpy system has been widely studied in various borylation reactions directed by steric^{6a,b,9} and/or electronic factors.^{6a,b,10} The use of numerous directing groups to achieve ortho selective arene borylation has also been developed using Ir¹¹ and Rh¹² catalytic systems. Despite the wide interest in this transformation, the absence of less costly metal catalytic systems is noteworthy. Ruthenium has been found to be highly active in a broad range of ortho arene functionalization through C-H activation reactions using different nitrogen- and oxygen-based directing groups.13 However, the ruthenium-catalysed ortho-borylation of sp² carbons is rare, and only a few examples have been described,14 using a very specific substrate at very high catalyst loadings (10-50 mol%)^{14a} and, more recently, in the borylation of indoles.14b

Taking up this challenge, at first, we began studying the solvent effect and the reactivity of the different ruthenium dihydridosilyl complexes (**2a–2d**) in the direct *ortho*-borylation of 2-phenylpyridine (Table 1), in the presence of 1 equiv. of bis(pinacolato)diboron. We tested various solvents in the presence of **2a** (2.5 mol%) (see ESI†). No product formation was detected in NMP, DMF and DMAc, and only low conversions were obtained when the reaction was carried out in toluene. Noteworthy, 1,4-dioxane shows a greatly beneficial effect on the reaction, leading to the formation of the desired borylated compound (**3a**) with full conversion. Lower temperatures (60 °C and 80 °C) were also tested, but under these milder conditions the



^{*a*} Reaction conditions: 3 (0.25 mmol), B_2pin_2 (0.25 mmol) and 2a (3.75 µmol, 1.5 mol%); 1,4-dioxane (0.5 mL). Isolated yields are average of at least two runs. ^{*b*} 75% conversion.

starting material was recovered unchanged. Ruthenium complexes **2b–e** showed much lower reactivity in the C–H activation reaction, reaching the desired product with only low conversions. It is remarkable that the loading of **2a** can be decreased to 1.5 mol% without any loss in conversion to the desired product. In order to compare the reactivity of our system with other ruthenium-based catalysts, dichloro(*p*-cymene)ruthenium dimer was tested (see ESI†). A less effective conversion of 76% was obtained under optimised reaction conditions (5 mol% of ruthenium and KOAc as additive), using the dimer, proving to be a less active system in the arene borylation compared to the use of our well-defined catalyst (**2a**).

Under the optimized reaction conditions, the scope of a series of substituted pyridyl and congener substrates was examined (Table 1). The borvlation of 2-phenylpyridine (3a) and benzo[h]quinolone (3b)proceeded with very good isolated yields (84-90%). Substituted pyridines with electron-donating or electron-withdrawing groups were successfully borylated. The presence of either an electrondonating (Me or OMe) or an electron-withdrawing (F) group at the para or meta position of the 2-phenylpyridine did not affect the reactivity and the desired borylated adducts were always obtained in good yields (80-83%) (4c-e and 4g-h). The presence of an ester group in either the para (3f) or meta (3i) position is also well tolerated, leading to the desired products in good yields (4f and 4i) accompanied with no change in regioselectivity. The ortho-borylation of 2-(naphthalene-1-yl)pyridine 3j did not take place to full conversion (75%), however, the desired product was isolated in moderate vield (65%) (4i).

Several experiments were conducted to probe the reaction mechanism. Unfortunately, we were unable to isolate the postulated ruthenium intermediate resulting from the activation of the phenylpyridine by 2. However, we were able to detect the formation of triethylsilane by ¹H-NMR and GC-MS in the stoichiometric reaction between 2a and 2-phenylpyridine (3a). In the course of our mechanistic studies, pinacolborane can be spectroscopically identified (¹H-NMR and ¹¹B-NMR) after the addition of (bis)pinacolatodiboron to the reaction mixture depicted in reaction a of Fig. 1 (as well as in every other crude reaction mixture generated).

On the basis of these observations and literature precedents,^{13,15} a mechanism involving reaction of the pyridine and **2a** generating the ruthenacycle **I** and HSiEt₃ is proposed. The ruthenium($_{IV}$) intermediate **I** then reacts with B₂pin₂ forming a new ruthenium($_{IV}$) intermediate (**II**), with concomitant release of HBpin.^{6e,16} Reductive elimination forming the desired borylated adduct, and the subsequent regeneration of intermediate **I** in the presence of a new molecule of pyridine closes the catalytic cycle. Further investigations are currently ongoing in our laboratory to better understand the mechanism of the hydrosilylation reaction and how this sequence can suggest novel reactivity mediated by **2**.

Finally, to test the compatibility of the method with other transformations,^{11*a*} the generated borylated product was directly launched in a Suzuki–Miyaura reaction. As can be seen in Scheme 2, the ruthenium-catalysed borylation and the palladium-catalysed Suzuki–Miyaura cross-coupling procedures,¹⁷ in a one-pot reaction, *via* sequential catalyst/substrate addition proceed very well



Fig. 1 Stoichiometric reactions and proposed catalytic cycle for the C–H bond borylation reaction.



leading to the desired final product 5 in good yield over two steps (80% overall yield) without isolation of the borylated product.

In conclusion, a new family of 3-phenylindenyl dihydridosilyl ruthenium complexes (**2a–e**) has been synthesized using a very straightforward protocol. In addition, for the first time, a practical and selective borylation of arene *ortho*-C–H bonds catalysed by a ruthenium catalyst has been developed. **2a** shows very high activity (1.5 mol%) and excellent regioselectivities in the borylation of pyridines. This catalyst represents an alternative to the existing and more expensive Ir and Rh catalytic systems that can also be used in tandem with other reactions, an example for the Suzuki-Miyaura reaction is illustrative. Extensions of the methodology to other substrate classes are presently being examined.

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